REMARKS

Status of the Claims

Claims 1-13, 15-31, 33-34, and 36-38 are pending with claims 1-5, 13, 15, and 22 being independent. Claims 3-4 and 15-21 have been withdrawn by the Examiner as being drawn to a non-elected species. A listing of the claims is provided for the Examiner's convenience. No claim amendments have been made.

Initially, Applicants would like to thank the Examiner for allowing independent claim 13 and broadening the search to encompass the compounds of formulae I, IA, and IB.

Applicants respectfully request the Examiner to reconsider and withdraw the outstanding rejections in view of the following remarks.

Claim Objections

Claims 23-31, 33-34, and 36-38 stand objected to under 37 C.F.R. 1.75(c) as being in improper form because they depend from claims 5, 13, and 15. Applicants respectfully disagree with this objection; therefore, this objection is respectfully traversed.

37 C.F.R. 1.75(c) states that a multiple dependent claim shall refer to other claims in the alternative only and shall not serve as a basis for any other multiple dependent claim. M.P.E.P. §608.01(n) further explains that a multiple dependent claim is a dependent claim which refers back in the alternative to more than one preceding independent or dependent claim and provides examples of acceptable multiple dependent claim wording. One such example is "Claim 5. A gadget as in ***any one of claims 1, 2, and 3***, in which --- (emphasis added)."

Applicants respectfully submit that claims 23-31, 33-34, and 36-38 are in proper form. Applicants' recitation of "[t]he method according to ***any one of claims 5, 13, and 15***, wherein... (emphasis added)" is acceptable multiple dependent claim wording as it refers back to preceding claims in the alternative and is exemplified as acceptable in the M.P.E.P. None of claims 23-31, 33-34, and 36-38 are a multiple dependent claim based upon a multiple dependent claim. Accordingly, withdrawal of the objection is respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 1-2, 5-12, 22-31, 33-34, and 36-38 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,489,300 ("Thorsett et al.") in view of U.S. Patent Application Publication No. 2002/0161006 ("Kawamura et al."). Applicants respectfully disagree with this rejection; therefore, this rejection is respectfully traversed.

Thorsett et al. discloses compounds defined by formulae I and IA as set forth at col 3., line 15-col. 5, line 22. Certain of the compounds inhibit, in vivo, adhesion of leukocytes to endothelial cells mediated by VLA-4 and, accordingly, can be used in the treatment of diseases mediated by VLA-4. Accordingly, Thorsett et al. further discloses pharmaceutical compositions including the compounds of Formulae I and IA, which can be used to treat inflammatory disorders such as inflammatory brain disorders. Col. 88, lines 29-31 and col. 95, lines 26-42.

Kawamura et al. discloses compositions comprising specific 1,4-dihydropyridine compounds that are antagonists of bradykinin ("BK") useful in the treatment of inflammation and a variety of conditions in which inflammation is a component of the condition. Page 1, paragraph [0001]. Such compositions can include the specific 1,4-dihydropyridine compounds, inhaled glucocorticoids (e.g. prednisone), and adhesion molecule inhibitors (e.g. VLA-4 antagonists). Page 12, paragraph [0200].

Independent claims 1, 2, 5, and 22 stand rejected. Independent claim 1 is directed to a method of ***promoting remyelination*** of nerve cells in a mammal comprising administering to the mammal in need thereof a compound in a ***remyelinating effective amount***, wherein the compound is of formula I. Independent claim 2 is directed to a method of ***promoting remyelination*** of nerve cells in a mammal comprising administering to the mammal in need thereof a compound in a ***remyelinating effective amount***, wherein the compound is of formula IA. Independent claim 5 is directed to a method of ***promoting remyelination*** of nerve cells in a mammal comprising administering to the mammal in need thereof a compound in a ***remyelinating effective amount***, wherein the compound is of formula IB. Independent claim 22 is directed to a method of ***promoting remyelination*** of nerve cells in a mammal comprising administering to the mammal in need thereof a compound in a ***remyelinating effective amount***, wherein the compound is selected from named compounds within the scope of formula I and IA.

In the Office Action, the Examiner alleges the combination of Thorsett et al. and Kawamura et al. read on the claimed methods of ***promoting remyelination***. The Examiner alleges:

> "The methods of Thorsett et al. and Kawamura et al. teach the methods for the treatment of multiple sclerosis. Thus, the disease process is disclosed and treated. Multiple sclerosis is known in the art as a demyelinating condition. ***Any method used to treat multiple sclerosis would treat and stop the disease progression, which would then allow for remyelination of diseased nerve cells***." (emphasis added)

Applicants respectfully submit the cited references, alone or in combination, do not disclose or suggest the claimed methods of ***promoting remyelination***. As noted above by the Examiner, the prior art discloses stopping disease progression. However, the prior art does not disclose or suggest promoting remyelination.

The claimed methods of promoting remyelination are directed to promoting repair and/or regeneration of the myelin sheath of nerve cells. Promoting remyelination is significantly different from stopping disease progression.

Applicants respectfully submit any method used to treat multiple sclerosis that treats and stops disease progression would treat and stop myelin degradation. However, stopping disease progression, including the loss of the myelin sheath, is distinct from promoting repair and/or regeneration of the myelin sheath. The knowledge that certain compounds are useful for treating and stopping myelin degradation would not lead one of ordinary skill in the art to understand that the compounds could be used to promote repair and/or regeneration of the myelin sheaths. In fact, industry thinking may be to the contrary.

Furthermore, Applicants respectfully submit the presently claimed methods of promoting remyelination are contemplated for use in treating a wide variety of conditions and diseases associated with demyelination, ***not only demyelinating conditions and diseases induced as a result of an inflammatory response***. The Examiner points to methods that treat and stop multiple sclerosis, which is an inflammatory disease. While multiple sclerosis happens to be a demyelinating disease, other diseases and conditions involve demyelination which is not induced as a result of an inflammatory response. Diseases and conditions involving demyelination, for which the claimed method of promoting remyelination is useful further include congenital

metabolic disorders (*e.g.*, phenylketonuria (PKU), Tay-Sachs disease, Niemann-Pick disease, Gaucher's disease, Hurler's syndrome, Krabbe's disease and other leukodystrophies), neuropathies with abnormal myelination (e.g. Guillain Barré, chronic immune demyelinating polyneuropathy (CIDP), multifocal CIDP, anti-MAG syndrome, GALOP syndrome, anti-sulfatide antibody syndrome, anti-GM2 antibody syndrome, POEMS syndrome, perineuritis, IgM anti-GD1b antibody syndrome), drug related demyelination (*e.g.*, caused by the administration of chloroquine, FK506, perhexiline, procainamide, and zimeldine), and other hereditary demyelinating conditions (*e.g.*, carbohydrate-deficient glycoprotein, Cockayne's syndrome, congenital hypomyelinating, congenital muscular dystrophy, Farber's disease, Marinesco-Sjögren syndrome, metachromatic leukodystrophy, Pelizaeus-Merzbacher disease, Refsum disease, prior related conditions, and Salla disease). Page 35, lines 8-24. For example, PKU, classical Tay-Sachs, and Gaucher's disease are due to enzyme deficiency and certain drugs and radiation induce demyelination in subjects. Page 38, lines 9-28, page 39, lines 11-20., page 41, line 12.

Applicants respectfully submit ***inflammation can be advantageous*** to the treatment of multiple sclerosis under certain conditions. ***Inflammation can stimulate remyelination.*** See Foote et al. (Inflammation stimulates remyelination in areas of chronic demyelination, Brain 128, 528-539)(2005) and Hohlfeld (Does inflammation stimulate remyelination?, J. Neurol (2007) 254 [Suppl 1]: I/47-I/54). Thorsett et al. discloses compounds known to be useful in treating inflammation. At the very least, the fact that inflammation can stimulate remyelination calls into question why one of ordinary skill in the art would use compounds which counter inflammation in order to attempt to stimulate remyelination. The fact that inflammation can stimulate remyelination may lead one of skill in the art away from attempting to use Thorsett et al.'s compounds to promote remyelination.

Moreover, Applicants respectfully submit the industry continues to search for therapies to promote remyelination. According to Dubois-Dalcq et al. (Enhancing Central Nervous System Remyelination in Multiple Sclerosis, Neuron, vol. 48, 9-12, 2005), "[w]hile therapies designed to reduce inflammation can decrease the disease burden, they do not directly address the question of myelin repair in chronic disease. Recent advances in the stem cell field, and in particular the biology of adult neural precursor cells, ***have raised hopes that remyelinating therapies may***

soon be developed...(emphasis added)" Thus, there is a long-felt, but unsolved, need for remyelinating therapies.

Additionally, Applicants respectfully submit Thorsett et al.'s compounds are administered in an ***amount effective to treat inflammation***. In contrast, the presently claimed methods of promoting remyelination involve administering the compounds in a ***remyelinating effective amount***.

Finally, Applicants contend the compounds of Thorsett et al. are not identical to the presently claimed compounds.

Accordingly, withdrawal of the obviousness rejections is respectfully requested.

Double Patenting Rejections

Claims 1-2 and 5 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20 and 21 of U.S. Patent No. 6,291,453 ("Ashwell et al."), claims 13 and 14 of U.S. Patent 6,362,341 ("Thorsett et al. 1"), claims 34 and 35 of U.S. Patent 6,492,421 ("Thorsett et al. 2"), claims 1 and 4 of U.S. Patent 6,939,855 ("Yednock et al."), claims 12 and 13 of U.S. Patent 7,030,114 ("Thorsett et al. 3"), claim 14 of U.S. Patent 7,288,526 ("Thorsett et al. 4"), and claims 1, 2, and 20 of U.S. Patent 7,320,960 ("Thorsett et al. 5") in view of Thorsett et al.

For at least the reasons as described above, Applicants respectfully request withdrawal of the obviousness-type double patenting rejections.

Conclusion

For the reasons noted above, the art of record does not disclose or suggest the inventive concept of the present invention as defined by the claims.

In view of the foregoing remarks, reconsideration of the claims and allowance of the subject application is earnestly solicited. In the event that there are any questions relating to this application, it would be appreciated if the Examiner could telephone the undersigned attorney concerning such arguments so that prosecution of this application may be expedited.

If necessary to affect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to affect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #103900-B100854).

Respectfully submitted,

CROWELL & MORING LLP

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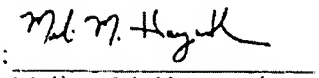
By: 

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